

Supplementary Figure S1A. Detailed description of scales included in the meta-analysis

Psychopathology:

Positive and Negative Syndrome Scale (PANSS) (Kay et al., 1987), Brief Psychiatric Rating Scale (BPRS) (Overall & Gorham, 1962), or Manchester Scale (MS) (Manchanda et al., 1986) total, positive symptom subscale, and negative symptom subscale, and Clinical Global Impression – Severity scale (CGI-S) (Guy, 1976) scores

Extrapyramidal Symptoms (EPSs):

Simpson-Angus Scale (SAS) (Simpson & Angus, 1970) total, Barnes Akathisia Rating Scale (BARS) (Barnes, 1989) total or global, Abnormal Involuntary Movement Scale (AIMS) (Guy 1976) total scores, and Drug-Induced Extrapyramidal Symptoms Scale (DIEPSS) (Inada, 1996) total scores

Neurocognitive function:

Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) (Randolph et al., 1998) total scale scores or MATRICS (Measurement and Treatment Research to Improve Cognition in Schizophrenia) Consensus Cognitive Battery (MCCB) (Nuechterlein et al., 2008) standardized total score

Quality of life (QOL)

S-QoL (Auquier et al., 2003), EuroQol 5 Dimension (EQ-5D) (Tsuchiya et al., 2002), EuroQol Health-Related Quality of Life (EuroQol-HRQOL) (EuroQol Group, 1990)

References

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Supplementary Figure S1B. Procedure to determine the cut-off of factors identified by the number of successful and unsuccessful studies

	Success	Failure	Not available
Factor $X > A$	a	b	c
Factor $X \leq A$	d	e	f
Not available	g	h	i

Notes: a~i, number of studies

The sensitivity is defined as $a/a+d$.

The specificity is defined as $e/b+e$.

A is considered a threshold when it gives the highest sensitivity and specificity (i.e. $\text{specificity} + \text{sensitivity} - 1$) in terms of the number of successful and unsuccessful studies.

Here is an example:

Factor	Cut-off, years	Sensitivity	Specificity	Sensitivity+Specificity-1
Age	36	16/19 (84.2%)	2/3 (66.7%)	0.509
	37	15/19 (78.9%)	2/3 (66.7%)	0.456
	38	15/19 (78.9%)	2/3 (66.7%)	0.456
	39	15/19 (78.9%)	2/3 (66.7%)	0.456
	40	14/19 (73.7%)	3/3 (100%)	0.737
	41	11/19 (57.9%)	3/3 (100%)	0.579
	42	9/19 (47.4%)	3/3 (100%)	0.474
	43	8/19 (42.1%)	3/3 (100%)	0.421
	44	7/19 (36.8%)	3/3 (100%)	0.368

Then, age of 40 years is considered a cut-off because it gives the highest sensitivity and specificity.

Supplementary Figure S1C. Definition of successful factors identified by the number of studies classified by outcome

	Success	Failure	Not available
Factor $X > A$	a	b	c
Factor $X \leq A$	d	e	f
Not available	g	h	i

Notes: a~i, number of studies

Factor X is considered a predictive factor for successful dose reduction if it meets both of the following criteria:

- (i) $a/(a+b) = 100\%$
- (ii) $e/(b+e+h) > 50\%$

Here is an example: There are 20 successful and 4 unsuccessful studies in total, and there are 14 successful studies and 0 unsuccessful studies with a mean age > 40 years, 5 successful and 3 unsuccessful studies with a mean age ≤ 40 years, and 1 successful and 1 unsuccessful studies not available for age.

	Success	Failure	Not available
Age > 40 years	14	0	0
Age ≤ 40 years	5	3	0
Not available	1	1	0

Then, age > 40 years is considered a predictive factor for successful dose reduction because it meets both of the following criteria:

- (i) $14/(14+0) = 100\%$
- (ii) $3/(0+3+1) > 50\%$

Supplementary Figure S1D. Decision and procedure of further subgroup analysis after subgroup analysis of effect estimate in relapse rate

Factors	Subgroup	Effect estimate	Overall effect
		[95% CI]	<i>P</i> -value
Factor Y	> A	a [b - c]	d
	≤ A	e [f - g]	h

A further subgroup analysis of studies with a factor $Y > A$ or factor $Y \leq A$ is conducted if it meets both of the following criteria:

- (i) Factor $Y > A$ or $\leq A$ is considered a predictive factor for successful / unsuccessful dose reduction if the corresponding overall effect *P*-value was either $d < 0.05$ or $h < 0.05$, respectively.
- (ii) Factor Y is relevant to antipsychotic dose.

Here is an example:

Factors	Subgroup	Effect estimate	Overall effect
		[95% CI]	<i>P</i> -value
Antipsychotic dose after reduction	> 200 mg/day	1.07 [0.57 - 2.02]	0.83
	≤ 200 mg/day	2.79 [1.29 - 6.03]	0.009*

A further subgroup analysis of studies with antipsychotic dose after reduction ≤ 200 mg/day is conducted because it meets both of the following criteria:

- (i) Overall effect *P*-value = 0.009 (i.e., < 0.05)
- (ii) Antipsychotic dose after reduction is related to relevant to antipsychotic dose.

Supplementary Figure S1E. Decision and procedure of sensitivity analysis of subgroup analysis

Factors	Subgroup	Effect estimate	Overall effect
		[95% CI]	<i>P</i> -value
Factor Y	> A	a [b - c]	d
	≤ A	e [f - g]	h

If there is a study which demonstrates Factor Y = A (i.e. just right on the threshold), the sensitivity analysis is conducted to see if the results are consistent in the following two comparisons to elucidate the robustness of the findings:

- (i) Factor Y > A or ≤ A
- (ii) Factor Y ≥ A or < A

Here is an example: if there is a study with a mean age of 40 years, we conduct the both of the following comparisons; mean age > 40 years and ≤ 40 years, and ≥ 40 years and < 40 years.

Factors	Subgroup	Effect estimate	Overall effect
		[95% CI]	<i>P</i> -value
Age	> 40 years	1.02 [0.50 - 2.07]	0.96
	≤ 40 years	2.56 [1.38 - 4.75]	0.003*
	≥ 40 years	1.38 [0.75-2.55]	0.30
	< 40 years	2.46 [1.16-5.24]	0.02*